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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,236	04/28/2006	Holger Winter	2923-741	2529

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EXAMINER	
STAPLES, MARK	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
08/19/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,236	WINTER ET AL.	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *10 and 13-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 11, 12, and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment of claim 7 and the submission of new claims 24 and 25 in the paper filed on 04/30/2008 is acknowledged.

Newly submitted claim 24 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the specie election filed on 11/02/2007 was to pyrimidine nucleotides. As claim 24 recites the limitation of pyrimidine nucleotide analog it is not the specie of the election.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 24 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-9, 11, 12, and 25 consonant with the specie election filed on 11/02/2007 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

2. It is noted that Applicant has not provided an English translation of the foreign German application 103 26 302.0. Accordingly, priority is not extended to the German application.

Objections that are Withdrawn

3. The objection to the specification is withdrawn in light of Applicant's amendments to properly identify the trademarks RHODAMINE GREEN™, BODIPY™, and ALEXA™.

4. The objection to claim 7 is withdrawn in light of Applicant's amendment of the claim to properly identify the trademarks.

Rejections that are Maintained

Claim Rejections Maintained - 35 USC § 112 Second Paragraph

5. The rejections of claims 1-9, 11, and 12 under 35 USC § 112 Second Paragraph is maintained. Applicant's arguments filed 04/30/2008 have been fully considered but they are not persuasive. Applicant argues that the terms "nucleotide analog" and "pyrimidine nucleotide analog" are well known in the art, but does not provide any evidence of this and does not provide any evidence of a list or a closed set of compounds for either of these terms that is universally accepted in the art. Thus one of ordinary skill in the art would not know the metes and bounds of these terms and the rejections are maintained. It is also noted that the limitation for pyrimidine nucleotide analog as recited in claim 24 is not found in claims 1-9, 11, and 12.

Claim Rejections Maintained - 35 USC § 103

6. The rejection of claims 1-9, 11, and 12 under 35 U.S.C. 103(a) as being unpatentable over Tyagi et al. (November 21, 2000), Weisburg et al. (August 29, 2000), and Nunnally et al. (1997) is maintained.

Applicant's arguments filed 04/30/2008 have been fully considered but they are not persuasive.

Applicant argues that Tyagi et al. do not teach probe termini ending in pyrimidines and teaches away from probe termini ending in pyrimidines. This is not so as Tygai et al. teach at least the synthetic sequence of SEQ ID NO. 2 in which one end has two cytosines (CC) which are pyrimidines and which sequence is double labeled with fluorophores (see Example 2). Thus Tyagi et al. teach towards probes ending in pyrimidines. There is no teaching of Tyagi et al. excluding probes ending in pyrimidines. Furthermore, Tyagi et al. is not relied upon alone for this teaching, Weisburg et al. is also relied upon as follows.

Applicant argues that Weisburg et al. does not teach sequences with both termini ending in pyrimdines. This is not so as Weisburg et al. teach SEQ ID NO: 2 having the pyrimidines of C on the 5' end and TTC on the 3 end (as found at column 4 line 48 and in the Sequence Listing). Weisburg et al. also teaches a specific sequence of 14 pyrimidines which are T's (see Figure 4) and thus where both the termini thus have multiple pyrimidines. Both of these sequences read on the formula for the generic Z of claim 1. The later sequence of Tayagi et al. reads on the formulae for the generic Z of claims 1 and new claim 25. It is also noted in these formulae of claims 1 and 25 that the middle nucleotides, the X's, can be any nucleotide, including T, and can be the same nucleotide as the Z's.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies

(i.e., exclusion of repetitious sequences) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant further argues that Weisburg et al. does not teach increased sensitivity using pyrimidine ending probes. Although such a teaching is not needed, as Weisburg et al. teach the elements of the claimed product, nonetheless Weisburg et al. do teach that pyrimidine ending probes increase sensitivity in the capture of target polynucleotides (entire patent, especially the Abstract).

Applicant argues Nunnally et al. does not teach all of the limitations of the claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

New Rejections Necessitated by Amendment

7. It is noted that newly submitted claim 25 differs from claim 1 by reciting a different range of integers of 3-10 for n. However as claim 25 is examined with respect to the same specie as claim 1 the same prior art is applicable as given below.

New Claim Rejection - 35 USC § 103

8. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tyagi et al. (United States Patent No. 6,150,097 issued November 21, 2000), Weisburg et al. (United States Patent No. 6,110,678 issued August 29, 2000), and Nunnally et al. (1997).

Regarding claims 25, Tyagi et al. teach a probe of formula (I) (see SEQ ID NO: 5 in column 13 lines 17-19)

where Z is the pyrimidine nucleotide C,

where M and M' are fluorescent groups which can be fluorescein (see Figure 4) and where M and M' are identical, that is the same, fluorescent group (see column 3 lines 45-48),

where in SEQ ID NO: 5 n is 1,

and m can be 7-140 and thus can be 40 (see claim 10).

Regarding claim 25, Tyagi et al. do not specifically teach a poly pyrimidine tail, that is, where n for Z is 5. Tyagi et al. do not specifically teach where the fluorophore labeling group is RHODAMINE GREEN™.

Regarding claim 25, Weisburg et al. teach where Z_n is at least C_5 by teaching C_n where n is at least about 10 bases (column 8 Lines 36-59). Weisburg et al. teach that fluorophores well known in the art can be used on probes, but do not specifically teach where the fluorophore labeling group is RHODAMINE GREEN™.

Weisburg et al. teach the further specie election of formula (II) where X is - O-; Y is =O; Y' is -OH; and R is –OH (see Structure 1 in column 13).

Weisburg et al. also teach thymidine 2' deoxynucleotides (see Example 1).

Fruther regarding the specie election, Weisburg et al. teach where Z_n is at least T_5 by teaching T_n where n is at least about 10 bases (column 8 Lines 36-59). Weisburg et al. also teaches a specific sequence of 14 pyrimidines which are T's (see Figure 4) and thus where both termini have multiple pyrimidines. This sequences read on the formula for the generic Z's and X's of claim 25. it is noted in this formula that the middle nucleotides, the X's, can be any nucleotide, including T, and that X and Z can be the same nucleotide.

Regarding claim 25 and the specie election, Nunnally et al. teach fluorescein, as also taught by Tyagi et al. above, and that RHODAMINE GREEN™ may be substituted for fluorescein (see Table 1 and see the 1st full paragraph in the 2nd column on p. 2394). Nunnally et al. teach that the use of fluorescein in probes was well known (see 1st full paragraph on p. 2392).

Tyagi et al. teach pyrimidine nucleotides on the ends of a probe and teach identical fluorophores including fluorescein on the ends of probes. Weisburg et al. teach multiple pyrimidine nucleotides on the ends of probes and fluorescent labels on the ends of these. Nunnally et al. teach that the use of fluorescein was well known and that RHODAMINE GREEN™ may be substituted for fluorescein. Because both Tyagi

et al. and Weisburg et al. teach well known fluorophores, it would have been obvious to one skilled in the art to substitute the well known fluorescein of Tyagi et al. as the fluorophore for the well known fluorophores of Weisberg to arrive at the claimed probe, but with fluorescein being the identical flurophore on each end (instead of RHODAMINE GREEN™). As Nunnally et al. teach RHODAMINE GREEN™ may be substituted for fluorescein, it would have been obvious to one skilled in the art to substitute RHODAMINE GREEN™ for the fluorescein of Tyagi et al. and Weisberg in order to achieve the predictable result of a probe having ends of poly pyrimidine nucleotides with RHODAMINE GREEN™ at the ends of each of these.

Conclusion

9. No claim is free of the prior art.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
/M. S./
Examiner, Art Unit 1637
August 8, 2008

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637